
Mitochondrial protection attenuates inflammation-induced impairment of neurogenesis in vitro and in vivo.

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Public Summary:

Scientific Abstract:

The impairment of hippocampal neurogenesis has been linked to the pathogenesis of neurological disorders from chronic neurodegenerative disease to the progressive cognitive impairment of children who receive brain irradiation. Numerous studies provide evidence that inflammation downregulates neurogenesis, with multiple factors contributing to this impairment. Although mitochondria are one of the primary targets of inflammatory injury, the role of mitochondrial function in the modulation of neurogenesis remains relatively unstudied. In this study, we used neurosphere-derived cells to show that immature doublecortin (Dcx)-positive neurons are uniquely sensitive to mitochondrial inhibition, demonstrating rapid loss of mitochondrial potential and cell viability compared with glial cells and more mature neurons. Mitochondrial inhibition for 24 h produced no significant changes in astrocyte or oligodendrocyte viability, but reduced viability of mature neurons by 30%, and reduced survival of Dcx(+) cells by 60%. We demonstrate that protection of mitochondrial function with mitochondrial metabolites or the mitochondrial chaperone mtHsp75/mortalin partially reverses the inflammation-associated impairment of neurogenesis in vitro and in irradiated mice in vivo. Our findings highlight mitochondrial mechanisms involved in neurogenesis and indicate mitochondria as a potential target for protective strategies to prevent the impairment of neurogenesis by inflammation.

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